REQUEST FOR RECONSIDERATION

Claims 1-8 remain active in this application.

The claimed invention is directed to a method for producing alkyl (3R, 5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3, 5-dihydroxy-6-heptenoate by **epimeric separation** by liquid chromatography treatment using **silica gel as the packing material**.

The rejections of claims 1-5 and 7 under 35 U.S.C. §102(a) and (b) and of claim 6 under 35 U.S.C. §103(a) over Ikeda et al., U.S. 5,939,552, Nagamatsu et al. (1999), Chen et al., U.S. 6,835,838 and Onishi et al., U.S. 6,946,557 are respectfully traversed.

None of the cited references discloses or suggests a method for producing the claimed compound by using silica gel as the packing material in a liquid chromatography in which epimers are separated.

Ikeda et al. describes optical resolution of a racemic mixture of an optically active mevalonolectone compound by means of a batch system chromatography which uses a column filled with a filler selected from a group consisting of particles of polysaccharide ester derivative, particles of a polysaccharide carbamate derivative and particles of a support which carries a polysaccharide ester derivative and/or a polysaccharide carbamate derivative (column 1, lines 51-58). The reference makes clear that the polysaccharide derivative is the solid support and that silica gel, amongst others may be used as a support for the polysaccharide derivative (column 6, lines 25-35). The reference fails to describe silica gel as the packing material.

Nagamatsu et al. describes separation of DOLE **racemic mixture** on slightly modified Chiralcel OF, 20μm (Daicel) (page 58, section 2.5. Columns). Chiralcel OF is cellulose tris (4-chlorophenyl carbamate) coated on a silica gel substrate. Chiralcel OF is not silica gel as the packing material.

Chen et al. at column 16, describe the use of Chiralpak AD. Chiralpak AD is amylose tris (3,5-dimethylphenyl carbamate) coated on a silica-gel substrate. Chiralpak AD is not silica gel as a packing material in a liquid chromatography treatment.

Onishi et al. describe the use of cellulose tris (4-chlorophenyl carbamate) supported on a carrier as a filler for liquid chromatography. Cellulose tris (4-chlorophenyl carbamate) is Chiralcel OF, and as discussed above is not silica gel as the packing material.

None of these chromatography supports are silica gel as a packing material. To the contrary, the packing materials are a polysaccharide ester derivative and/or polysaccharide carbamate derivative which are **coated onto the surface of a silica gel**. There is no exposed surface of silica gel in these packing materials such that the silica gel is not a liquid chromatography packing material.

In contrast, the claimed invention is directed to a method in which silica gel as the packing material is used in liquid chromatography to separate epimers.

The examiner asserts that the art teaches silica gel as the packing material and that the instant claims do not differ silica gel alone from silica gel as an inorganic base. (page 3, line 3 from the bottom to page 4, line 1).

However, applicants' specification, at page 11, line 22, through page 12, line 1 describes the undesirability of using a packing material other than silica gel stating that the inclusion of impurities such as metals or **organic substances** is undesired. As the packing materials of the cited references are all organic substances coated onto the surface of silica gel, it is clear that applicants' use of the term "silica gel as a packing material" does not include a silica gel which is coated with an organic substance.

In addition, applicants respectfully submit that the use of silica gel as a support material does not suggest use of silica gel **as a packing material** as those of skill in the art recognize the term "silica gel as a packing material" to mean that **the surface** of silica gel **is**

used, relying on differences in adsorptivity with the surface of the silica gel, a phenomena which is not possible when silica gel is used as a support material.

As evidence of the meaning of the term "silica gel as a packing material" applicants enclose herewith a passage from chapter 8 of R. Adams, J. Johnson and C. Wilcox, *Laboratory Experiments in Organic Chemistry, seventh edition* (1979), entitled "Chromatography", in which the technique of liquid-solid chromatography is described as a process in which

> "[s]olid surfaces adsorb thin layers of foreign molecules as a result of forces identical in character with those operating between molecules of a liquid or of a gas. Since adsorption strengths differ with the character of the solid surface, a properly chose solid may adsorb selectively one component of a mixture."

The attached pages from the web site of Column Engineering of Ontario, California, a manufacture of columns and accessories for HPLC, identifies packing material differences as based on 1) silica structure; 2) silica chemistry; and **3) bonding chemistry**. The term "bonding chemistry" refers to the previously described forces which provide adsorption selectivity.

The attached pages from the web site of Merck KGaA of Darmstadt, Germany, differentiates between silica gel and derivatized silica gel (e.g. silanized silica gel) as it is clear that the two materials will provide vastly different adsorption properties to a foreign material.

These passages make clear that a packing material is identified in order to characterize the nature of the solid **surface** to which foreign molecules are being adsorbed.

Moreover, the cited reference or Ikeda et al. makes clear that they do not use silica gel as the packing material, as the examples of the support may be particles of polymers such as polystyrene, polyacryamide, polyacrylate, silica gel, alumina, magnesia, zirconia, glass, kaolin, titanium oxide, silicate salts, diatomaceous earth (column 6, lines 25-33). In view of

the vastly different natures of surfaces of these support materials, it is clear that the support materials are not being used as the packing material in a liquid chromatography, but rather are only a support, in which the surface of the support plays no role in the separation process.

Thus, those of ordinary skill in the art would clearly recognize the term "silica gel as the packing material" to refer to the use of a packing material in which **the surface** of silica gel is exposed to epimers of the compound of formula (1) resulting in differences in adsorption resulting in separation of the two epimers. Those of skill in the art would not recognize the term "silica gel as the packing material" to refer to a derivatized silica gel, as there is no surface of silica gel which is exposed to the epimers of formula (1) in order to provide differential adsorption. The term "silica gel as the packing material" does not refer to a derivatized silica gel in which silica gel is only a support material for another compound as the identity of the support material is of no critical concern, relative to the concern over the nature of the material which is interacting with the material being separated.

Further, none of the references describe separation of epimers of the claimed compound.

Each of the cited references describes optical resolution of entantiomeric mixtures of compounds. As entantiomeric mixtures, the compounds being separated are identical but for the absolute stereochemistry of the two enantiomer. The compounds are mirror images. The two enantiomers will have equal but opposite degrees of rotation when subjected to plane polarized light. The mixture of enantiomers being separated by Ikeda et al. is the 3R,5S and 3S,5R enantiomeric pair. These compounds have the same relative stereochemistry at the 3 and 5 stereocenters.

In contrast, the claimed process is one in which epimers are separated. Epimers are compounds which differ in relative stereochemistry at one stereocenter. Epimers are not mirror images. Moreover their behavior to plane polarized light need not be of equal but

opposite degrees of rotation. As discussed in applicants' previous response the mevalonolactone compounds of 3R,5S and 3R,5R represent the pair of epimers of the claimed process. The relative stereochemistry between 3 and 5 positions of the 3R, 5S epimer **differs** from that of the 3R, 5R epimer.

Contrary to the examiner's position taken on pages 4 and 5 the separation of enantiomeric mixtures, in which the compounds only differ in absolute stereochemistry, does **not** include the separation of epimers, in which the compounds differ in relative stereochemistry. (see above for an explanation of the differences between enantiomers and epimers).

As the cited reference fails to disclose or suggest using **silica gel as the packing material** in a liquid chromatography treatment nor the separation epimers, the claimed invention is clearly neither anticipated nor rendered obvious by this reference and accordingly withdrawal of the rejections under 35 U.S.C. §102(b) and 35 U.S.C. §103(a) is respectfully requested.

Applicants submit this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

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Laboratory Experiments in ORGANIC CHEMISTRY

SEVENTH EDITION

Roger Adams
LATE OF THE UNIVERSITY OF ILLINOIS

John R. Johnson
CORNELL UNIVERSITY

Charles F. Wilcox, Jr.
CORNELL UNIVERSITY

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8

Chromatography

The term chromatography is applied to numerous purification processes that share the principle of distributing a sample between a stationary phase and a mobile one. As with extraction, the degree of separation of a mixture is determined by differences in distribution coefficients, which are related to the same structural factors controlling solubility.

Liquid-Solid Chromatography

Solid surfaces adsorb thin layers of foreign molecules as a result of forces identical in character with those operating between molecules of a liquid or of a gas. Since adsorption strengths differ with the character of the solid surface, a properly chosen solid may adsorb selectively one component of a mixture. An important example of selective adsorption is the use of charcoal in crystallization to remove colored impurities. The ideal limiting law governing adsorption from a dilute solution is:

$$\frac{[\text{Amount of Solute } A \text{ Adsorbed per Unit Surface Area}]}{[\text{Concentration of Solute } A \text{ in Solution}]} = K_A$$

The factors that determine the extent of adsorption of a molecule on a solid surface are closely related to the factors that enter into solubility considerations. An additional complication in adsorption is that the solvent and the solute are competing for the active sites on the surface. For molecules containing polar functional groups the value of K_A (the adsorption coefficient) is determined principally by the relative polarities of the substance and the solvent. Highly polar solvents tend to be preferentially adsorbed, so that a low K_A results for the solute. For molecules containing hydroxyl groups their relative abilities to form hydrogen bonds (proton-bonding) to the solid or the solvent are significant.

Two solutes having different adsorption coefficients toward a certain solid can be separated by the process of liquid–solid chromatography. One of the most practical methods involves preparation of a cylindrical column of the solid (*stationary phase*) and addition of a concentrated solution (*liquid phase*) at the top of the column. As the solution penetrates the column the solutes are adsorbed. At the moment the solution has completely penetrated the column, fresh solvent is added at the top. The solvent flows down the column and redissolves the solutes in amounts determined by the adsorption law and carries them to lower clean sections of the column, where they are readsorbed (in amounts governed by the adsorption law). As more solvent percolates through the column, the cycle of adsorption–solution continues, and the solutes gradually move down the column in concentrated bands (*development*). With solutes having different adsorption coefficients the least tightly adsorbed material tends to move ahead more readily. If the coefficients are sufficiently different or the column is sufficiently long the faster moving component will form a separate band below the slower moving one. At the lower end the solutes are forced off the column (*elution*) and can be collected separately in successive fractions.

For satisfactory separation by liquid–solid column chromatography it is essential to choose an appropriate combination of solid adsorbent and eluent that is compatible with the compounds to be separated. Compounds that are adsorbed very tightly require an excessive volume of eluent for development. Compounds adsorbed weakly may move too rapidly to give separation before being eluted. Table 8.1 gives some generalizations that are useful as a guide in selecting appropriate solid–solvent combinations.

A common variation of liquid–solid chromatography is the use of a thin film of solid (mixed with a binder such as plaster of Paris) on a sheet of glass or plastic. The solution is added as a spot at the bottom of the plate and the plate dipped vertically into a shallow layer of solvent, which ascends by capillary action and moves the solutes with it. The particular advantage of this technique is that the solutes are exposed and can be isolated readily or treated on the plate at any moment. The method is widely used for qualitative identification of mixture components because of its exceptionally good resolution. For a fixed combination of solid, binder, and solvent each substance will travel along the thin-layer plate a characteristic fraction of the distance traveled by the solvent. It is customary to report thin-layer chromatography data as R_f values (retention factor) defined as the distance of the spot from the starting point divided by the distance of the solvent front from the starting point. Thin-layer chromatography is restricted to small samples. A method known as dry-column chromatography, which combines the high resolution of thin-layer chromatography with the large sample capacity of regular column chromatography, is described under Laboratory Practice.

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TABLE 8.1
Generalizations for Liquid–Solid Chromatography

SOLIDS IN DECREASING ORDER OF ADSORPTION STRENGTH FOR POLAR MOLECULES
Activated Alumina,* Charcoal
Activated Magnesium Silicate*
Activated Silicic Acid*
Inorganic Carbonates
Sucrose, Starch
SOLVENTS IN INCREASING ORDER OF ELUTING ABILITY†
Saturated Hydrocarbons
Aromatic Hydrocarbons
Ethers
Halogenated Hydrocarbons
Ketones
Alcohols
Organic Acids

* The adsorption strength can be diminished by addition of water. Under carefully controlled conditions, this strength is reproducible.

† This approximate order only applies to alumina. With nonpolar solids, the order tends to be inverted.

Figure 8.1 shows the distribution of sample along the length L of a chromatography column or a thin-layer plate. The position of maximum concentration when the solvent just reaches the end occurs at length l from

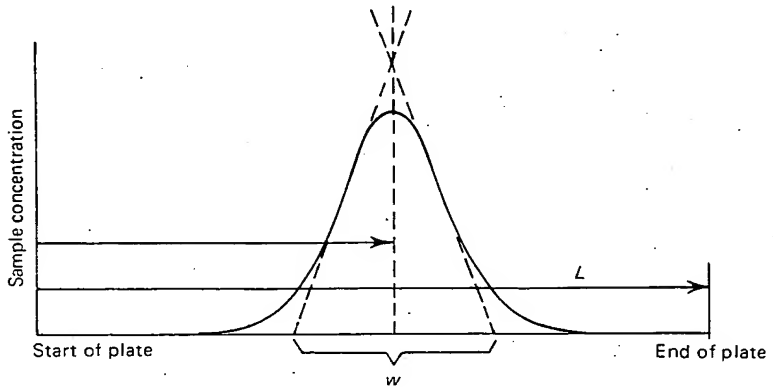


Figure 8.1. Chromatographic Sample Distribution

the starting point. By definition $R_f = l/L$; it can be demonstrated that R_f is also equal to $n/1 + K$ where K has the definition given at the beginning of this section and n is the average number of effective exchanges of a molecule of the sample on and off the surface in the time it takes the solvent front to traverse the column or plate.[1] For tightly retained samples, K is very large and n is small. For the ideal case it has been shown that

$$n \cong 16\left(\frac{l}{w}\right)^2 \tag{1}$$

where w is the width at the base of the triangle formed by drawing straight lines through the most linear portions of the sample distribution curve as shown in Figure 8.1.

A more recent innovation in liquid–solid chromatography is to use finely divided solids, which provide an exceptionally high surface area for a given weight of solid.[2] The effective number of exchanges in a given length of column is larger because of the small particle size, and hence for a particular value the peak width is correspondingly smaller in accordance with equation 1 for n. The practical drawback to packing a chromatography column with fine adsorbent is that the flow rate is then extremely slow. The problem was overcome by the development of essentially surgeless solvent pumps that allow the chromatograph to be developed under pressures as high as 1000 psi at the inlet. With such equipment remarkable analytical and preparative separations of complex mixtures have been obtained. Much less expensive low-pressure chromatographs (pressures up to about 100 psi at the inlet) show intermediate advantages and are gaining popularity in research laboratories.

Ion-Exchange Chromatography

Ion-exchange chromatography is a special example of liquid–solid chromatography, wherein strong ionic attractions replace relatively weak polar adsorption forces.

A column of solid acidic material (such as Amberlite IR-120, a resin of polystyrene beads containing free sulfonic acid groups) can donate protons to any bases present in the surrounding liquid phase to form cations and anions that strongly attract each other. The extent of proton transfer depends on the basicity of the solute and can be described by an equilibrium constant K (analogous to the previously discussed adsorption coefficient).

[1] Some workers use the reciprocal of this definition of K, in which case, $R_f = nk'/1 + k'$, where $k' = 1/K$.

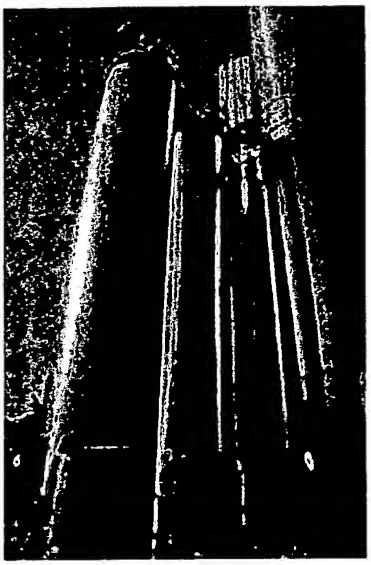
[2] The surface area of a given weight of spheres increases as the inverse of their radius.

Standardized Silica Gels

The basis for reproducible chromatography in laboratory and production Preparative column chromatography is consistent sample and chromatographic variables. One of the most difficult variables for a user to control is of course the stationary phase.

In practice, standardized sorbents are required. These will provide a high degree of method reliability, direct transfer from analytical scale and allow carefully optimized throughput per unit of time.

Only silica gels with a defined pore structures and reproducible trace component profiles fulfill the requirements of chromatography.



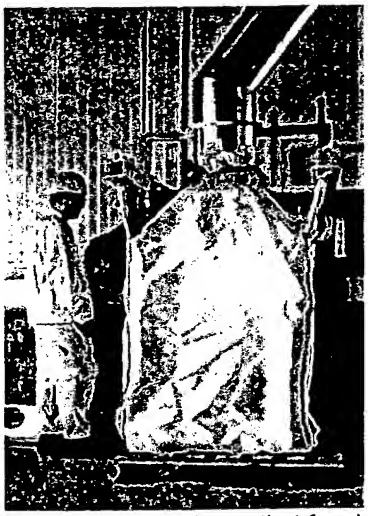
Merck KGaA, Darmstadt, Germany, has specialized, for decades, in the manufacture of standardized silica gel packing materials for preparative chromatography and offers a wide range of customized sorbents. The product range is extensive with several special types, e.g. silica gels such as LiChroprep® to high purity acid-washed silica gels.

Merck KGaA gels provide the user with unique diversity of methodology: Regardless of which chromatographic process is used (DC, TLC, HPTLC, HPLC, preparative chromatography), direct and rapid transfer to a production scale is guaranteed and with minimized risk. This is ensured by the fact that common base raw materials are used for all stationary phases, thus providing identical chromatographic selectivity.

In order to be able to achieve this goal, Merck produces all silica gel 60 packing materials for analysis, pilot plant processes and production using the same silica gel raw material which has specified surface area and a defined specific pore volume and pore size distribution.

Once a particular silica gel raw material has been tested with respect to its suitability for pore structure, specific pore volume, specific surface, chemical purity and other requirements for chromatography, it is classified into defined particle size ranges.

These particle size ranges are selected to optimize the separating performance and permeability results for the chromatographic process used (DC, TLC, HPTLC, HPLC, preparative chromatography).



Thus, once a successful separation has been found at the analytical scale, it can be transferred rapidly to pilot plant or production scale (see illustration below).

Merck KGaA, Darmstadt, Germany, standardized Silica Gels thus offer direct scale-up without compromise and without lost time.

The selectivity of Merck's silica gels for analytical and preparative applications is identical. Resolution, however, decreases, according to theory, with increasing particle size. Improved separation can be achieved at the expense of longer retention times and if the selectivity of the entire system is optimized using different mobile phases.

Merck KGaA Quality: customized without compromise, for a high degree of reliability in production.

Experience has shown that for chromatographic separations in production, silica gel 60 i.e. silica gels with a mean pore size of 60Å and in particle size ranges 40-63µm and 63-200µm are precisely suited to the separation of complex mixtures.

Specifications

	Silica Gel 60 (40-63µm)	Silica Gel 60 (63-200µm)
Catalog Number	9385	7734
Particle Size Range (µm)	40-63µm	63-200µm
Mean Particle Size (µm)	~50	~105
Specific Surface Area (m2/g)	~500	~500
Specific Pore Volume (ml/g)	0.70-0.78	0.71-0.78
Mean Pore Size (Å)	60	60
pH (10% aqueous suspension)	7±0.5	7±0.5
Loss on Drying (%) (3 hours/120°C)	<9	<7
Bulk Density (g/ml)	~0.45	~0.45
Back Pressure (bar) (column 250-4, n-heptane, 20ml/min)	~2	~0.5
Iron (%) (acid extraction)	<0.02	<0.02
Chloride (%) (acid extraction)	<0.02	<0.02
Theoretical Plates (N/m)*	~3000 (anisole)	~1000 (anisole)
Relative Retention Alpha*	~1.73	~1.73

* 2-nitroanisole/4-nitroanisole

Standard Silica Gel Ordering Information

Description	Cat. No.	Particle Size	pH	Package	Contents
Silica Gel 40	1.10180.1000 1.10180.5000	63-200 µm (70-230 mesh ASTM)	5.5±0.5	Plastic	1 kg 5 kg
Silica Gel 40	1.10181.1000 1.10181.9025	200-500µm (35-70 mesh ASTM)	5.5±0.5	Plastic	1 kg 25 kg
Silica Gel 60	1.15111.1000 1.15111.2500 1.15111.9025	15-40µm	7.0±0.5	Plastic	1 kg 2,5 kg 25 kg
Silica Gel 60	1.09385.1000 1.09385.2500 1.09385.5000 1.09385.9025	40-63µm (230-400 mesh ASTM)	7.0±0.5	Plastic	1 kg 2,5 kg 5 kg 25 kg
Silica Gel 60	1.07729.1000 1.07729.5000 1.07729.9025	< 63µm (>230 mesh ASTM)	7.0±0.5	Plastic	1 kg 5 kg 25 kg
Silica Gel 60	1.15101.1000 1.15101.9025	63-100µm (170-230 mesh ASTM)	7.0±0.5	Plastic	1 kg 25 kg
Silica Gel 60	1.07734.1000 1.07734.2500 1.07734.5000 1.07734.9025	63-200µm (70-230 mesh ASTM)	7.0±0.5	Plastic	1 kg 2,5 kg 5 kg 25 kg
Silica Gel 60 extra pure	1.07754.0500 1.07754.1000	63-200µm (70-230 mesh ASTM)	7.0±0.5	Plastic	500 g 1 kg
Silica Gel 60	1.07733.0500 1.07733.1000 1.07733.5000 1.07733.9025	200-500µm (35-70 mesh ASTM)	7.0±0.5	Plastic	500 g 1 kg 5 kg 25 kg
Silica Gel 100	1.10184.0500 1.10184.5000	63-200µm (70-230 mesh ASTM)	6.5±0.5	Plastic	500 g 5 kg
Silica Gel 100	1.10185.0500 1.10185.9025	200-500µm (35-70 mesh ASTM)	6.5±0.5	Plastic	500 g 25 kg
Silica Gel 60 F254	1.10757.1000	63-200µm (70-230 mesh ASTM)	7.0±0.5	Plastic	1 kg

Derivatized Silica Gels

These products are all based on our proven and standardized silica gels for production chromatography. Starting material is a silica gel with a nominal pore diameter of 60Å that has been effectively used over many decades.

The silanized silica gel (Cat. No. 7719) is a material that has been slightly deactivated by dimethylsilyl groups and which has a high specificity for the separation of very polar, acid or strongly lipophilic substances. This material is comparable in polarity with RP-2 material and can be placed between an RP-8 and a cyano-phase.

Silica gel 60 RP-18 (40-63µm) (Cat. No. 10167) is a stationary phase modified with C18 groups and is ideal for the purification of compounds of molecular weight lower than 1,000 Daltons in semi-preparative and preparative scale.

The Ideal Reversed Phase Material for Production Scale

An alternative material to non-modified silica gel because non-toxic solvents in the RP-mode are used.
For the economic purification of products where conventional RP-phases were too expensive.
High loading capacity due to its high specific surface area of the base silica gel (60Å pore diameter, approximately 500m2/g); therefore column dimensions/amount of sorbent can be reduced or the sample volume increased.
High pressure stability under extreme production conditions for long-term column usage.

Specifications: Silica Gel 60 RP-18 (40-63µm) for Preparative HPLC

Particle Size	90% between 40 and 64µm
Elementary Analysis	15-20% C
Elutable Fraction	<0.2%
Mean Pore Size	60Å

Selectivity Test

k-value (Benzene) 7.2-10.8
alpha = Acetophenone/Phenol 1.7-2.3
alpha = Acetophenone/Cinnamic acid 1.1-1.5
alpha =Naphthol/Phenol 3.6-4.6

Comparison of Selectivity Profile

	LiChroprep® RP18 (40-63µm)	Silica Gel 60 RP-18 (40-63µm)
k-value (Benzene)	7.65-10.35	7.2-10.8
alpha=(1)Acetophenon/Phenol	1.9-2.1	1.7-2.3
alpha=(2)Acetophenon/Cinnamic Acid	1.23-1.36	1.1-1.5
alpha=(3)Naphthol/Phenol	3.8-4.2	3.6-4.6

Comparison of Different Stationary Phases show the following values under identical chromatgraphic conditions:

Stationary Phase	alpha (1)	alpha (2)	alpha (2)	k (benzene)
LiChrospher® RP-18 (12µm)	2.1	1.36	3.8	10.3
LiChrosorb® RP-18 (7µm)	1.98	1.28	3.8	9.8
LiChroprep® RP-18 (40-63µm)	2.0	1.28	3.8	10.2
Silica Gel 60 RP-18 (40-63µm)	2.3	1.50	3.87	10.6

Description	Particle Size	Cat. No.	Package	Quantity

Silica Gel 60 Silanized*	63-200µm	1.07719	Glass	250g
Silica Gel 60 Silanized*	63-200µm	1.07719	Glass	1kg
Silica Gel 60 RP-18**	40-63µm	1.10167	Glass	100kg

* (dimethylsilane derivate) (70-230 mesh ASTM)
** (230-400 mesh ASTM)

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Site Map

Column engineering offers hplc packings, hplc packing materials, liquid chromatography, reliasil, monitorc18 columns, intersil, kromasil, gc columns, shperisorb, and various other chromatography materials.

C.E. Facts	Literature Request	Special Offer	Ordering Specifics	Packing Material Differences	Packing Material Selection	Fastener Seperations: Resolution vs. Column Length
Column Selection Criteria	Special Offer	Related Links	Hypersil	Inertsil	Kromasil	Monitor
pH Protection: Why use Gaurd Cartridges?	USP Categories For HPLC Columns	Resiasil	Spherisorb	HPLC Packings	Sensitivity/Solvent Sonsumption: 3mm vs. 4.6mmID	Nucleosil

Make your selection from below:

COLUMN ENGINEERING INCORPORATED

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Packing Material Differences

Silica-based packing materials that belong to the same category (i.e.C18/USP L1) do not necessarily provide equal chromatography when made by different manufacturers.

For instance, two different 5µ C18 150x4.6mmID columns used for the same method may provide quite different results in terms of resolution, selectivity, efficiency, and peak shape due to the following material differences:

Silica Structure: Surface Area Pore - Volume Pore-Size/Distribution - Particle Size/Distribution

Silica Chemistry: Silanol Frequency - Silanol Types - Silica Surface Acidity

Bonding Chemistry: Type of Functional Group - Method of Bonding - Bonded Group Concentration

Minor differences between packing materials can create major differences in chromatography, but the following relationships generally apply for reversed phase chromatography:

Increased Surface Area → Increased Retention Times

Increased Carbon Load →
Increased Retention Times

Lower Surface Acidity →
Improved Peak Symmetry

Packing Material Selection

If a specific material is specified for your method, choose it from your preferred supplier. Otherwise, start out with a column from a suggested category (C8, C18, etc.) in a standard size such as a 150 x 4.6mm.

Once you have optimized your method for this first column, you can determine what parameters or conditions you may be able to change to improve your chromatography.

For general changes in column selection, refer to the next section, *Column Selection Criteria*. If your selection requires knowledge of specific differences between packings, call us for technical assistance.

Step1: Select Column Criteria

Brand Name: Hypersil, Inertsil, Spherisorb, Kromasil, Nucleosil, etc.

Classification: Hypersil **BDS**, Inertsil **ODS-2**, Kromasil **100Å**, Nucleosil **300-5**, etc.

Bonded Phase: C8, C18(ODS, ODS-2), Phenyl, etc.

Material Lot#: It is provided with each Column Engineering column delivered.

Column Size: 150 x 4.6mm, 150 x 3.9mm, 250 x 4.6mm, etc.

Step2: Select Column Source

Choose a column manufacturer that understands packing materials from the ground up. As mentioned, many column suppliers do not control or manufacture their own base materials. They purchase bulk packings and pack the columns. This makes a world of difference in having control over the critical supply of base material in terms of choices available, consistency, and uninterrupted supplies. **Column Engineering** is a bulk silica manufacturer and a

great source for all you column supply needs.

C.E. Facts	Literature Request	Special Offer	Ordering Specifics	Packing Material Differences	Packing Material Selection	Fastener Seperations: Resolution vs. Column Length
Column Selection Criteria	Special Offer	Related Links	Hypersil	Inertsil	Kromasil	Monitor
pH Protection: Why use Gaurd Cartridges?	USP Categories For HPLC Columns	Resiasil	Spherisorb	HPLC Packings	Sensitivity/Solvent Sonsumption: 3mm vs. 4.6mmID	Nucleosil

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